+1L

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/607,719	06/27/2003	Likan Liang	02-850-CIP	9414

34704 7590 09/03/2004

BACHMAN & LAPOINTE, P.C.
900 CHAPEL STREET
SUITE 1201
NEW HAVEN, CT 06510

EXAMINER	
TRAN, SUSAN T	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 09/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/607,719	LIANG ET AL.	
	Examiner	Art Unit	
	Susan T. Tran	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/22/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of applicant's Response to Notice File Missing Parts, Request for Corrected Filing Receipt, and Oath filed 02/05/04, and Information Disclosure Statement filed 10/22/03.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3, 5-9, 12, 13, 17 and 19 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10, 12 and 13 of copending Application No. 10/324,954 ('954) in view of Chen et al. US 6,267,985 (Chen). Application '954 claims a formulation for stabilized capsule for oral administration of hydrophobic pharmaceutically active agent comprising a non-aqueous solubilizer selected from 2-pyrrolidone, N-alkylpyrrolidones and combinations thereof; and a capsule stabilizing agent selected from mono-, di- and triglycerides, mono- and di-fatty esters of polyethylene glycol, fatty acids and combinations thereof. Solubilizer is N-methyl-2-pyrrolidone or 2-pyrrolidone is found in claims 2 and 3.

Amounts of stabilizing agent with respect to the non-aqueous solubilizer are found in claims 7-9. Application '954 is silent to the teaching of the weight ratio between fibrate and solubilizer, however, absent of evidence on the contrary, it is the position of the examiner that it would have been obvious for one of ordinary skill in the art to, by routine experimentation select the claimed ratio because a 1:1 to 1:100 ratio is a wide range of ratio. Application '954 does not explicitly claim fenofibrate and the use of surfactant, however, specification at page 14, lines 1-2 of application '954 disclosed "the hydrophobic pharmaceutically active agent is fenofibrate". Application '954 claims combination of stabilizing agents, such as mono-, di- and triglycerides, mono- and di-fatty esters of polyethylene glycol and fatty acids. Chen teaches hydrophobic surfactant includes fatty acids and polyethylene glycol fatty acid esters (column 26, lines 32-67). Chen also teaches hydrophobic surfactants are compounds having HLB value less than about 10 (column 8, lines 35-41). Thus, in view of the combination of application '954 and Chen, one of ordinary skill in the art would expect a similar formulation of fenofibrate. There are no unusual and/or unexpected results which would rebut prima facie obvious. As such, the instant claims would have been obvious given the claims of application '954, which set out a similar formulation using the same ingredients, namely, combination solubilizer that includes fatty acid, mono-, di- and triglycerides, mono- and di-fatty esters of polyethylene glycol (surfactant), as claimed herein.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-3, 6, 9, 10, 12-15 and 19 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-21 of copending Application No. 10/324,953 ('953). Although the conflicting claims are not identical, they are not patentably distinct from each other because application '953 claims an oral pharmaceutical formulation of a fibrate with improved oral bioavailability comprising fenofibrate, derivative or mixtures thereof, dissolved in one or more fibrate solubilizers selected from N-alkyl derivative of 2-pyrrolidone, mono- or di- or polyethylene glycol monoether, C_{8-12} fatty acid mono- or diesters of propylene glycol, or combinations thereof, and one or more surfactants selected from nonionic, anionic, cationic, and zwitterionic surfactants and combinations thereof, wherein the fibrate to the solubilizer weight ratio is between about 1:1 and about 1:100. Self-emulsifying formulation is found in claim 4. Diethylene glycol monoethyl ether is found in claim 11. Therefore, one of ordinary skill in the art would expect the same formulation of fenofibrate from the use of the claimed invention given the claims of application '953. There are no unusual and/or unexpected results, which would rebut prima facie obvious. As such, the claimed invention would have been obvious given the claims of '953, which set out a similar formulation of combination of hydrophobic active agent, solubizing agent, and stabilizing agent.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 6, 9, 10, 14, 17 and 20-22 are rejected in the use of the phrase "mono- or di- or polyethylene glycol". It is unclear what this compound is?

Claim 7 is rejected in the use of the phrase "selected from mixtures of...combinations thereof; with one or more...or combinations...and fatty acids". It is confusing and unclear as to what mixtures and what combination is intended. Further clarification is suggested.

Claim 18 recites the limitations "the C_{max}" and "the AUC" in lines 1 and 2. There is insufficient antecedent basis for these limitations in the claim. Claims 1, 9 and 17 do not recite C_{max} and AUC.

Claims 20-22 are rejected in the use of the phrase "the surfactant is about 2 W/W%, and about 25 W/W%". The range amount of surfactant is unclear. Further clarification is suggested.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Laruelle US 5,827,536, in view of Chen et al. US 6,267,985.

Laruelle discloses a pharmaceutical dosage formulation comprising fenofibrate dissolved in a solubilizing agent of diethylene glycol monoethyl ether (DGME). The weight ratio of DGME and fenofibrate is between 10 and 20, which is 1:2, and would fall within the claimed range of 1:1 to 1:100 (column 3, lines 20-22; claims 2 and 7). The formulation further comprises additives capable of increasing the solubilizing power of DGME and/or of increasing the stability of the solution (column 3, lines 23-33). The formulation is administered for the treatment of hypercholesterolaemias and hypertriglyceridaemias (column 2, lines 52-58). Laruelle also teaches a process for improving the bioavailability of fenofibrate by dissolving fenofibrate in DGME (column 3, lines 55-67).

Laruelle is silent as to the teaching of additional ingredients, such as, surfactant, and stabilizing agent.

Chen teaches a pharmaceutical composition comprising hydrophobic therapeutic agent including fenofibrate (column 28, lines 40-49; and column 29, line 66); at least two surfactants selected from hydrophilic and hydrophobic surfactants (column 26, lines 32-51); and mixtures of solubilizers (column 34, lines 29-30). Hydrophobic surfactant is compounds having HLB value less than about 10 (column 8, lines 35-41) that includes fatty acids (column 26, lines 52-67); and hydrophilic surfactant is compounds having

HLB greater than 10 (ID). Solubilizers include polyvinyl alcohol, cellulose derivatives, 2-pyrrolidone, and N-methylpyrrolidone (column 34, lines 5-17). The composition further comprises other additives, such as binders, fillers, viscomodulators, and mixtures thereof (column 35, lines 43-52). The pharmaceutical composition is formulated as preconcentrate in a liquid (column 35, lines 54-57). Thus, it would have been obvious for one of ordinary skill in the art to modify the composition of Laruelle using the additional ingredients in view of the teachings of Chen, because Laruelle teaches a fenofibrate formulation comprises solubilizer and other additives capable of increasing the solubilizing power of DGME and of increasing the stability of the composition (ID), because Chen teaches the use of solubilizer to enhance the solubility of hydrophobic drug (column 33, lines 63-65), because Chen teaches combination of surfactants can solubilize therapeutically effective amounts of therapeutic agents in homogeneous systems, which are a thermodynamically stable and optically clear (column 4, lines 58-61), and because Chen teaches the composition that enhanced rate and/or extent of absorption of the therapeutic agent (column 5, lines 1-3). The expected result would be a stable preconcentrate formulation of fenofibrate in combination with triglyceride, mixture of surfactants, and mixture of solubilizing agents.

It is noted that the references do not explicitly teach the amounts of all the ingredients. However, Generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges

by routine experimentation. *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Therefore, it is the position of the examiner that it would have been obvious for one of ordinary skill in the art to, by routine experimentation determine suitable amounts of ingredients with the expectation of at least similar result, because the references teach similar pharmaceutical composition the same compound, namely fenofibrate, using similar solibilizer, similar stabilizing agent, as well as similar surfactants, for the same use, *e.g.*, for the treatment of hyperlipidaemias and hypertriglyceridaemias.

Regarding the Cmax and the AUC, the burden is shifted to applicant to show that the formulations taught by the cited prior arts do not exhibit the claimed Cmax and AUC. The PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product. Whether the rejection is based on inherency' under 35 U.S.C. 102, on prima facie obviousness under 35 U.S.C. 103, jointly or alternatively, the burden of proof is the same...[footnote omitted]. *In re Fitzgerald*, 619 F.2d 67, 70, 205 USPQ 594, 596 (CCPA 1980). See also *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Applicant's attention is called to Laruelle at column 1, lines 1-10 discloses formulations exhibit a significantly improved bioavailability or "superbioavailability". Chen at column 4, lines 66 through column 5, lines 1-3 discloses formulations that result in an enhanced rate and/or extent of absorption of the therapeutic agent.

Pertinent Arts

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Al-Ghazawi et al., Bossies et al., Deboeck et al., Crooks et al., Dong et al., Moussa et al., and Hauer et al. are cited as of interest for the teachings of capsule formulation.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan T. Tran whose telephone number is (571) 272-0606. The examiner can normally be reached on M-R from 6:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page, can be reached at (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

S. Tran
Patent Examiner
AU 1615